Q FEVER

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

While up to 60% of infections are asymptomatic, symptomatic infections present in two distinct forms: acute, which occurs just after initial exposure; and chronic, which can occur years after an initial infection. Acute infection may present as a non-specific febrile illness, with severe headache, myalgia, malaise, weakness, chills, severe sweating, and anorexia. Pneumonia or hepatitis occurs in up to 60% of acutely ill persons. The illness resolves gradually over 1–4 weeks, and life-threatening sequelae such as endocarditis and meningoencephalitis are rare.

The chronic form of the disease is characterized by infection that lasts for more than six months. This form is far less common—occurring in less than 1% of infected persons—but more serious. Chronic Q fever may develop any time between 1–20 years after the initial infection. The most serious complication of chronic disease is endocarditis: infection of the valves of the heart. Patients with pre-existing valvular disease, cancer, and chronic kidney disease are at greater risk for the development of the chronic form of Q fever.

Causative Agent:

Q fever is a bacterial disease caused by *Coxiella burnetii*. *C. burnetii* is classified as a rickettsiae and is an intracellular pathogen. The organism is very stable and is highly resistant to many disinfectants.

Differential Diagnosis:

Symptoms are non-specific and diagnosis can be delayed. This disease can be mistaken for other chronic febrile illnesses such as plague and brucella.

Laboratory identification:

Laboratory diagnosis of Q fever is usually made serologically. Testing for IgM serology and PCR are not widely available, therefore diagnosis is made through a rise in IgG titer found in acute and convalescent sera. In addition, *C. burnetii* has two antigenic phases and shifts between them as the infection proceeds. Phase II antibodies predominate in the acute phase, whereas Phase I antibodies predominate in the chronic phase.

> **UPHL:** The UPHL can provide diagnostic capabilities for this organism during threat events. Typical clinical isolates should be routed through larger reference laboratories.

Treatment:

Acute disease treatment is usually doxycycline or a quinolone for 2-3 weeks. Chronic disease treatment should be guided by an infectious disease specialist.

Case fatality:
Approximately 1–2% of acute cases are fatal. The fatality rate for chronic Q fever is as high as 65%.

Reservoir:
Goats, sheep, and cattle appear to be the most important animal reservoirs. Other potential reservoirs include: dogs, cats, feral rodents, and birds. Ticks appear to be important in maintaining the disease reservoir within animals and some birds. However, direct human infection from a tick bite is rare.

Transmission:
Infected animals are usually asymptomatic, but they shed large numbers of organisms in placental tissue and amniotic fluid. The *C. burnetii* bacterium is most commonly transmitted through breathing in dust contaminated with dried placental material, birth fluids, or excrement from infected animals. Direct contact with infected animals or contaminated materials, such as straw, fertilizer, and laundry, is also a mode for transmission. *C. burnetii* has an extremely low infectious dose. A single inhaled organism may be enough to cause infection. *C. burnetii* is resistant to heat, drying, and many common disinfectants. The organism's ability to persist in the environment may result in a continued risk for infection weeks to months after an animal's birthing event. In rare cases, human infections have been reported to occur via intradermal injection, blood transfusion, and transplacentally. Transmission through ingestion of raw milk of infected cows or by tick bites is rare.

Susceptibility:
All people are susceptible to Q fever, however, certain professions are at higher risk. For example, veterinarians, meat workers, sheep (occasionally dairy) workers, and farmers. Also, those who work in stockyards, meatpacking and rendering plants, laboratories and in medical and veterinary centers that use sheep in research.

Incubation period:
The incubation period for acute Q fever varies, but it is generally 2–3 weeks. Signs and symptoms of chronic Q fever may develop anytime from 1–20 years after exposure.

Period of communicability:
Direct person-to-person transmission of Q fever is rare.

Epidemiology:
Q fever is a zoonotic disease that occurs worldwide. Human infection is presumably underreported. People with regular contact with sheep, goats, or cattle—such as veterinarians, meat processing plant workers, sheep and dairy workers, or livestock farmers—have the highest risk of exposure. In farming areas, seasonal disease trends occur with predictability, with the greatest increase in cases occurring around the lambing season during early spring.

Utah has had only 2 cases in the past 10 years (5-yr average of 0.2)

Bioterrorist Potential

C. burnetii is listed by the Centers for Disease Control and Prevention (CDC) as a Category B bioterrorist agent. If acquired and properly disseminated, *C. burnetii* could cause a serious public health challenge.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Identify the source of infection and prevent further transmission.
- Rule out the possibility of bioterrorism; Q fever is a category B agent.
- Check laboratory workers to assure that there was no exposure to the isolate, or that exposed laboratory personnel are appropriately treated.
- Notify the Department of Food and Agriculture if case was acquired in Utah.

Prevention:

- Assure appropriate disposal of placenta, birth products, fetal membranes, and aborted fetuses at facilities housing sheep and goats.
- Restrict access to barns and laboratories used in housing potentially infected animals.
- Use only pasteurized milk and milk products. Use appropriate procedures for bagging, autoclaving, and washing of laboratory clothing.
- Vaccinate (where possible—see below) individuals engaged in research with pregnant sheep or live *C. burnetii*.
- Quarantine imported animals.
- Ensure that holding facilities for sheep are located away from populated areas. Animals should be routinely tested for antibodies to *C. burnetii,* and measures should be implemented to prevent airflow to other occupied areas.
- Counsel persons at highest risk for developing chronic Q fever, especially persons with pre-existing cardiac valvular disease or individuals with vascular grafts.

Chemoprophylaxis:

Chemoprophylaxis following potential exposures is generally not recommended. Exposed populations may be monitored by public health or Department of Agriculture.

Vaccine:

A vaccine for Q fever is only available through military sources at Fort Detrick in Maryland. The vaccine is strongly recommended for those knowingly working with live *C. burnetii* in a laboratory setting. It may be considered for slaughter house workers and others in hazardous occupations.

Persons wishing to be vaccinated should first have a skin test to determine a history of previous exposure. Individuals who have previously been exposed to *C. burnetii* should

not receive the vaccine because severe reactions, localized to the area of the injected vaccine, may occur. A vaccine for use in animals has also been developed, but it is not available in the U.S.

Isolation and quarantine requirements:
None

✓CASE INVESTIGATION

Reporting:
- Report all suspect and confirmed cases of Q fever.
- Q fever is a category B BT agent

Case Definition:
Q fever *(Coxiella burnetii)* (2007):

Clinical presentation
Acute infection: Acute fever usually accompanied by rigors, myalgia, malaise, and retrobulbar pain (severe headache behind the eyes). Fatigue, night-sweats, dyspnea, confusion, nausea, diarrhea, abdominal pain, vomiting, non-productive cough, and chest pain have also been reported. Severe disease can include acute hepatitis, atypical pneumonia with abnormal radiograph, and meningoencephalitis. Clinical laboratory findings may include elevated liver enzyme levels, leukocytosis, and thrombocytopenia. Asymptomatic infections may also occur.

Note: Serologic profiles of pregnant women infected with acute Q fever during gestation may progress frequently and rapidly to those characteristic of chronic infection.

Chronic infection: Infection that persists more than 6 months. Potentially fatal endocarditis may evolve months to years after acute infection, particularly in persons with underlying valvular disease. Infections of aneurysms and vascular prostheses have been reported. Immunocompromised individuals are particularly susceptible. Rare cases of chronic hepatitis without endocarditis, osteoarthritis, and pneumonitis have been described.

Clinical evidence
Acute Q fever: Acute fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzyme levels.

Chronic Q fever: Newly recognized, culture-negative endocarditis, particularly in a patient with previous valvulopathy or compromised immune system, suspected infection of a vascular aneurysm or vascular prosthesis, or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology.

Laboratory evidence

Acute Q fever

Laboratory confirmed:

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer to *C. burnetii* phase II antigen by indirect immunofluorescence assay (IFA) between paired serum samples, (CDC suggests one taken during the first week of illness and a second 3-6 weeks later, antibody titers to phase I antigen may be elevated or rise as well) **or**
- Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, **or**
- Demonstration of C. burnetii antigen in a clinical specimen by immunohistochemical methods (IHC), **or**
- Isolation of *C. burnetii* from a clinical specimen by culture.

Laboratory supportive:

- Has a single supportive IFA IgG titer of ≥1:128 to phase II antigen (phase I titers may be elevated as well).
- Has serologic evidence of elevated IgG or IgM antibody reactive with *C. burnetii* antigen by enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Chronic Q fever

Laboratory confirmed:

- Serological evidence of IgG antibody to *C. burnetii* phase I antigen ≥1:800 by IFA (while phase II IgG titer will be elevated as well; phase I titer is higher than the phase II titer), **or**
- Detection of *C. burnetii* DNA in a clinical specimen via amplification of a specific target by PCR assay, **or**
- Demonstration of *C. burnetii* antigen in a clinical specimen by IHC, **or**
- Isolation of *C. burnetii* from a clinical specimen by culture.

Laboratory supportive:

- Has an antibody titer to *C. burnetii* phase I IgG antigen ≥1:128 and <1:800 by IFA

Note: Samples from suspected chronic patients should be evaluated for IgG titers to both phase I and phase II antigens. Current commercially available ELISA tests (which test only for phase 2) are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent (resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used. For acute testing, CDC uses in-house IFA IgG

testing (cutoff of ≥1:128), preferring simultaneous testing of paired specimens, and does not use IgM results for routine diagnostic testing.

Serologic test results must be interpreted with caution, because baseline antibodies acquired as a result of historical exposure to Q fever may exist, especially in rural and farming areas.

Exposure

Exposure is usually via aerosol, is broadly interpreted, and may be unknown (especially for chronic infection), but often includes the presence of goats, sheep, or other livestock, especially during periods of parturition. Direct contact with animals is not required, and variable incubation periods may be dose dependent.

Case classification

Confirmed acute Q fever: a laboratory confirmed case that either meets clinical case criteria or is epidemiologically linked to a lab confirmed case.
Probable acute Q fever: a clinically compatible case of acute illness (meets clinical evidence criteria for acute Q fever illness) that has laboratory supportive results for past or present acute disease (antibody to Phase II antigen) but is not laboratory confirmed.
Confirmed chronic Q fever: a clinically compatible case of chronic illness (meets clinical evidence criteria for chronic Q fever) that is laboratory confirmed for chronic infection.
Probable chronic Q fever: a clinically compatible case of chronic illness (meets clinical evidence criteria for chronic Q fever) that has laboratory supportive results for past or present chronic infection (antibody to Phase I antigen).

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.
- The sample must be confirmed by UPHL or the CDC in order to confirm the case.

Outbreaks:

An outbreak is defined as more than 1 case in a 30 day period.

Identification of case contacts:

This disease is rarely spread person-to-person. However, laboratory workers may become exposed during the culture and identification process. Public health should contact the testing laboratory(s) to see whether any personnel were exposed.

Case contact management:

All exposed laboratory workers should be referred to an infectious disease physician for appropriate antibiotic management.

✓REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Massachusetts Department of Health Q fever Disease Plan